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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,270	08/30/2000	Catharina Svanborg	032313-003	4240

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EXAMINER

HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 09/10/2002

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/555,270

Applicant(s)

SVANBORG, CATHARINA

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 11-23 is/are pending in the application.
- 4a) Of the above claim(s) 15,16,18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11-14, 17 and 20-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. The response to the restriction requirement mailed May 17, 2001 (Paper No. 15) is acknowledged. The restriction requirement set forth in Paper No. 15 is hereby **withdrawn**.

2. Claims 1-5 and 11-23 are pending.

Claims 15, 16, 18 and 19, drawn to non-elected inventions (original restriction), are withdrawn from consideration.

Claims 1-5, 11-14, 17 and 20-23 are examined on the merits.

Objections and Rejections Withdrawn:

3. The objection to the specification because it lacks most of the appropriate section headings is withdrawn in light of the amendment filed January 11, 2002.

4. The objection to claim 6 is withdrawn.

5. This application is now in compliance with the conditions of 35 U.S.C. 120.

6. The rejection of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendment filed January 11, 2002.

The rejection of claim 14 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, is withdrawn in light of the amendment filed January 11, 2002.

7. The rejection of claims 1 and 8 under 35 U.S.C. 103(a) as being unpatentable over Ming (Ming, L.-J., Magnetic Resonance in Chemistry 31: S104-S109, 1993; cited in the IDS) is withdrawn in light of the amendment to claim 1.

8. The rejection of claims 1-4, 6, 7, 11, 14 and 17 under 35 U.S.C. 103(a) as being unpatentable over Hakansson et al (Hakansson, A. et al, Proc. Natl. Acad. Sci., USA, 92: 8064-8068, 1995; cited in IDS) in view of Blair and Ghose (Blair, A.H. and T.I. Ghose, J. of Immunological Methods, 59: 129-143, 1983) is withdrawn in light of the amendment to claim 1.

9. The rejection of claims 1, 5 and 11 under 35 U.S.C. 103(a) as being unpatentable over Hakansson et al (Hakansson, A. et al, Proc. Natl. Acad. Sci., USA, 92: 8064-8068, 1995; cited in IDS) in view of Puri et al (U.S. 5,614,191; issued Mar. 25, 1997) is withdrawn in light of the amendment to claim 1.

10. The rejection of claims 1 and 8-10 under 35 U.S.C. 103(a) as being unpatentable over Hakansson et al (Hakansson, A. et al, Proc. Natl. Acad. Sci., USA, 92: 8064-8068, 1995; cited in IDS) in view of Johnstone and Thorpe (Immunochemistry in Practice, Blackwell Scientific Publications, Oxford, 1987; pages 113-130) and also in view of Goers (Goers, J.

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Immunochemical Techniques Laboratory Manual, Academic Press, New York, 1993; pages 69-79) is withdrawn in light of the amendment to claim 1.

Claim Rejections Maintained and New Grounds of Rejection:

11. The rejection of claims 14 and 17 under 35 U.S.C. 112, first paragraph, is maintained.

This rejection is newly made for claims 1-5, 11-13, and 20-23. The specification, while being enabling for methods of treating cancer with an agent of claim 1, where the agent is directly applied to a tumor, does not reasonably provide enablement for methods of treating cancer where the agent of claim 1 is administered in any fashion to the patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is drawn to an agent comprising a protein complex comprising multimeric α -lactalbumin and a cytotoxin. Thus, the agents of claim 1 encompass multimeric α -lactalbumin in combination with a cytotoxin, where the multimeric α -lactalbumin and the cytotoxin form a protein complex. The arguments supplied by applicant in arguing the merits of the prior art rejections appear to make the case that multimeric α -lactalbumin may be used as a targeting agent. Applicant also supplies a copy of an unpublished manuscript. Applicant's arguments have been carefully considered, but are unpersuasive.

The use of multimeric α -lactalbumin as a targeting agent, when the agent comprising multimeric α -lactalbumin is administered to a patient in any fashion, is not supported by the specification. The specification teaches that multimeric α -lactalbumin binds to all of the cells tested, including non-cancer cells (see page 21). Additionally, Hakansson (Proc. Natl. Acad.

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Sci., USA, 92: 8064-8068, 1995; cited in IDS) teaches the same thing (page 8068). Thus, multimeric α -lactalbumin does not appear to be an effective targeting agent. The specification does teach that multimeric α -lactalbumin by itself preferentially kills cancer cells, because multimeric α -lactalbumin preferentially enters the nuclei of cancer cells and not the nuclei of non-cancer cells. However, the preferential killing of cancer cells by entering nuclei does not provide the requisite targeting function for the claimed agents, because the agents comprise any cytotoxic agent that may be toxic in any compartment of any cell. Once multimeric α -lactalbumin is combined with a cytotoxic agent and binds to either a cancer cell or a non-cancer cell, both cells will be exposed to the cytotoxic agent regardless of the fact that multimeric α -lactalbumin only enters the nuclei of cancer cells. The breadth of claim 1, and the methods that depend from claim 1, includes agents where the cytotoxic agent may act in any compartment of a cell. Therefore, the practical usefulness of multimeric α -lactalbumin as a targeting agent for cytotoxic agents appears limited to methods where tumor cells are directly injected with the claimed agents, because multimeric α -lactalbumin appears to only be useful for transporting a cytotoxic agent into the nucleus of a cancer cell.

The specification appears to fail to teach examples of in vivo experiments demonstrating effectiveness of multimeric α -lactalbumin in a complex with a cytotoxic agent for the treatment of cancer. The unpublished manuscript provided by applicants is unpersuasive because the manuscript concerns the use of multimeric α -lactalbumin by itself as a cytotoxin, and does not provide evidence of multimeric α -lactalbumin in a complex with another cytotoxin. Thus, without working examples demonstrating in vivo efficacy, the specification fails to establish that

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the claimed agents and methods of treatment may be made and used by one of skill in the art in which any of the agents encompassed by claim 1 are used.

12. The rejection of claims 1, 11-13 under 35 U.S.C. 102(b) as being anticipated by Sabharwal et al (WO 96/04920; published 22 February 1996; cited in IDS) as evidenced by Kuwajima (Kuwajima, K., FASEB Journal, 10: 102-109, 1996; cited in IDS) is maintained.

The rejection is maintained because Sabharwal teaches multimeric α -lactalbumin, which may itself be a protein complex with a cytotoxic agent that has yet to be characterized.

13. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Hakansson et al (Hakansson, A. et al, Proc. Natl. Acad. Sci., USA, 92: 8064-8068, 1995; cited in IDS) as evidenced by Kuwajima (Kuwajima, K., FASEB Journal, 10: 102-109, 1996; cited in IDS) is maintained and newly applied to claim 17.

The rejection is maintained because Hakansson teaches multimeric α -lactalbumin (see page 8065, 1st to 2nd column), which may itself be a protein complex with a cytotoxic agent that has yet to be characterized. Hakansson teaches that multimeric α -lactalbumin has been administered to tumor cells (page 8065, 1st to 2nd column). Thus, Hakansson teaches the claimed inventions.

Conclusion

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
September 7, 2002


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